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Factors related to vitamin D deficiency in students of medicine in Gran Canaria

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Summary

Introduction: The bone-related and non bone-related functions of vitamin D are becoming better known by the day. As a result, levels of 25 hydroxyvitamin D (25-HCC) above 30 ng/mL are considered optimum.
Objectives: To study in a population of medical students in Gran Canaria what nutritional and lifestyle factors are associated with high levels of 25-HCC.
Material and method: A transverse study carried out in 98 Medical students of both sexes at the University of Las Palmas de Gran Canaria. All completed a questionnaire about their lifestyles and nutritional habits. A general physical examination was carried out and blood in fasting was taken to determine various biochemical parameters, including markers for remodelled bone, PTH and 25-HCC. In addition, bone mineral density was determined by dual X-ray absorptiometry and using ultrasound parameters in the calcaneum.
Results: We did not find statistically significant differences between thestudents who had levels of 25-HCC higher than 30 ng/mL and those with levels below this figure, in any of the variables studied, with the exception of male sex and the consumption of vitamin supplements.
Conclusions: Male gender in students of medicine in Gran Canaria, and the consumption of vitamin supplements, are associated with levels of vitamin D lower than 30 ng/mL.

Key words: *Vitamin D, Optimum levels, Young people, Students, sun, Exercise, Canary Islands, 25 hydroxycholecalciferol.*

Introduction

Vitamin D has a crucial role in bone metabolism, being responsible for the intestinal absorption of calcium and for bone mineralisation[1]. However, in recent years, in addition to being recognised as having an important role in the prevention and treatment of osteoporosis, many extra-bone actions have been described: reduction in risk of infections and autoimmune diseases, increase in muscle power, reduction in risk of suffering neoplasias of the colon, breast and prostate, improved control of diabetes, and preventing the appearance, or improving the course, of other diseases[2-13].

In the last few years a debate has developed around what are the optimum levels of vitamin D. Its metabolite, 25 hydroxyvitamin D (25-HCC) is considered to be the best indicator of the state of vitamin D reserves. Some authors have come to recommend optimum figures of 75 ng/mL of 25-HCC[14]. Others, such as Heaney, consider optimum levels to be those higher than 32 ng/mL[15], and as a consequence of this, a broad current of opinion has developed which situates the optimum levels of vitamin D as those in which 25-HCC is above 30 ng/mL, especially when referring to its extra-bone actions[1,16-19].

Nowadays, levels of vitamin D (25-HCC) are considered to be optimum when the values of 25-HCC are above 30 ng/mL, with the majority of authors considering that there is an insufficiency when these levels are below 30 ng/mL and a deficiency when levels are lower than 20 ng/mL[1,17-19]. However, in a high proportion of the population, both in patients and in healthy subjects, levels are found below these values.

The students of medicine of the University of Las Palmas de Gran Canaria (ULPGC) would theoretically be in ideal conditions for having optimum values of vitamin D, given that the climate of Gran Canaria is very sunny, with an annual average for sunshine of 2,750 hours, with the total average daily level of solar radiation in January being 3.1 kWh/m^2 and in July, 5.5 kWh/m^2,[20], and that the students are young, healthy and have theoretical knowledge regarding the vitamin D metabolism and the consequences of a deficit. However, in a previous study[21], we found that only 38.8% of the students of medicine of ULPGC, (42.1% of the males and 44.9% of the females), showed values of 25-HCC higher than 30 ng/mL, observing a deficiency in vitamin D in 32.6%, and an insufficiency in 61.2%, of the students.

Thus, in this work we have tried to identify what nutritional and life style variables could be associated with optimum levels of vitamin D.

Material and method

This is a transversal study, carried out in students of medicine in the Faculty of Health Sciences of ULPGC. The universe consisted of the totality of medical students in this faculty (620 in the 2007-8 course). All were invited to participate in this study, without restrictions. 103 students signed up, from all the courses, and gave their informed consent at the moment of completing the questionnaire, described later. There were two students from whom it was not possible to take blood, and another three who were not included because they did not complete the questionnaire or did not attend an appointment to determine their bone mineral density. 98 students completed the study.

Questionnaire. Physical examination

All the participants were asked to complete a questionnaire, which was self-completed, in which data was gathered on nutritional and lifestyle habits, with special attention paid to activity related to exposure to sun. All were weighed in light clothes and their height measured. The collection of data and the extraction of blood were completed over three days in May 2008.

The body mass index (BMI) was obtained using the formula: BMI: weight/height^2 (kg/m^2).

Collection of samples and laboratory techniques

The blood and urine samples were collected in the morning between 8.00 and 9.00 hours, after a night of fasting. The blood was collected in the correct tubes for each specific test, with the least vein compression possible, centrifuged at 1,500 g for 10 minutes, the serum separated in aliquots and stored within an hour of extraction at -20° C until the biochemical analysis was carried out, although most of these were carried out on the same day as the extraction.

The glucose, urea, creatinine, calcium, inorganic phosphorus, total protein, total cholesterol and its fractions and triglycerides were measured using automated techniques in an auto-analyser (Kodak Ektachem Clinical Chemistry Slides).

The blood calcium was corrected in accordance with the total proteins, by means of the formula:

Corrected calcium: Previous calcium (mg/dl)/[0.55 + total proteins (g/L)/16]

The tartrate resistant acid phosphatase (TRAP) was determined by spectrophotometry. Parathyroid hormone (PTH), 25-HCC, beta-crosslaps, osteocalcin, and PINP were determined through immunochemiluminscence.

Measurement of bone mineral density

The bone mineral density (BMD) was measured in the lumbar spine and in the proximal extremity of the femur with a Hologic QDR 1000 (Hologic Inc. Waltham, USA) densitometer. All the measurements were carried out by the same technician so that there were no interobserver variations. The coefficient of variation in our centre is 0.75 ± 0.16% with a range which varies between 0.6-1.13%[22]. The T-score values were calculated using the values of normality previously established for the Spanish population[23].

Determination of ultrasounds in the calcaneum

The ultrasound parameters in the calcaneum in the dominant foot were estimated by means of a Sahara© Hologic©(Bedford, MA, USA) ultrasound machine. This apparatus measures both the broadband ultrasound attenuation (BUA) and the speed of sound (SOS) in the area of interest of the calcaneum. The BUA and SOS combine in a single parameter called the quantitative ultrasound index (QUI), known also as the consistency index, which is obtained by means of the formula:

$$QUI = 0.41(SOS) + 0.41(BUA) – 571$$

Statistical study

This study has as its aim the identification of those factors which are associated with optimum levels of vitamin D. To this end, starting with the determination of the marker (blood levels of 25-HCC), the subjects were classified as having, or not having, an ideal level, according to whether the level of the marker was or was not above 30 ng/mL. In each of the groups in the study, the numerical variables were summarised as an average and SD, or as a median and IQR, according to whether or not they assumed normality, while the categorical were summarised as percentages.

In order to identify factors associated with the main objective, a multidimensional logistic regression analysis was carried out. Included in the analysis were all the variables which showed an association with $p< 0.1$, and all those which were related to frequent exposure to the open air (hiking, sport and walking in the open air). A retrospective selection of variables was carried out using the likelihood ratio test. A variable was kept in the model when the corresponding p-value was less than 0.1. The logistic model obtained is summarised in p-values and adjusted odd-ratios which were estimated by means of confidence intervals at 95%. The results of the analysis are then summarised in tables.

Results

Table 1 shows the number of students included in each group. A total of 60 subjects had levels of 25-HCC lower than 30 ng/mL, forming group I, or the group with insufficient levels. The 38 remaining, whose levels of 25-HCC were equal to, or greater than, 30 ng/mL made up the non-deficit group, or the group with optimum levels. The study was carried out in the month of May. There were no statistically significant differences between the two groups in terms of age, weight, height, BMI or waist measurement. The proportion of males who had insufficient levels of vitamin D was statistically higher ($p= 0.05$).

Table 2 lists the descriptions of the nutritional and lifestyle habits of the students who formed part of the study. There were no statistically significant differences in the distribution of these parameters between the students who had levels of 25-HCC higher than 30 ng/mL and those in whom it did not reach these levels. The only difference found was a tendency to a higher use of vitamin complexes among those students who had levels of 25-HCC lower than 30ng/mL, $p= 0.07$.

Table 3 shows the results obtained by comparing a series of biochemical parameters: kidney function, liver function, lipids, cholesterol and its fractions, triglycerides, glucose and ions. No statistically significant differences were found in any of these cases.

In Table 4 we present the data corresponding to the biochemical markers for remodelled bone (MRB), as well as p¡aratiroidea hormone (PTH) and the stimulating hormone of the thyroid (SHT).

In Table 5 we present the densitometric values. The bone mineral density (BMD) was estimated in the lumbar spine (L2-L4) and in the proximal extremity of the femur, in the femoral neck, the trochanter, the intertrochanter and the whole hip. In all these cases there were no statistically significant differences in the values obtained for the students in the two groups.

Table 6 shows the results of the logistic regression analysis. It can be observed that both the male sex and the consumption of vitamin supplements are inversely associated with optimum levels of vitamin D. Although the consumption of coffee appears to be protective and there seems to be a higher number of hikers the differences do not reach statistically significant levels.

Discussion

At present, there is a notable controversy about what are the optimum levels of vitamin D. Not many years ago values below 8 ng/mL of 25-HCC were considered as "severe deficiency", but more recently, optimum values of vitamin D have been considered to be those which prevent an increase in PTH and the development of secondary hyperparathyroidism (HPT)[25,26]. Even though up until now no consensus document has been published which advises on minimum desirable values of 25-HCC, there is a current trend to consider this to be 30 ng/mL[1,2,14-16,19,25].

We carried out the current study in a population of medical students of the ULPGC, because we consider that it could be considered as a "model" population for having optimum levels of vitamin D, for various reasons. First, because they are young and healthy, second, because due to their studies they know about the physiology of vitamin D and the ways of obtaining it, and third, because the place in which they reside, Gran Canaria, with its geographic proximity to the equator, situated at a latitude of 27 57 31 N°, has many hours of sun a year[20]. However, in analysing the prevalence of hypovitaminosis D in Canarian students, we found that only 38.8% of the students of medicine of the ULPGC, (42.1% of the males, and 44.9% of the females) showed values of 25-HCC higher than 30 ng/mL, with an insufficiency in vitamin D (less than 30 ng/mL) being observed in 61.2% of the students and vitamin D deficiency (less than 20 ng/mL) in 28.6% of them[21].

Table 1. Baseline characteristics of the population studied, classified as a function of blood levels of 25-HCC

	Insufficient levels n = 60	**Optimum levels n = 38**	**Value of p**
Age (years)	22.2 ± 3.3	22.4 ± 3.9	0.781
Man/woman (%)	36.7 / 63.3	18.4 / 81.6	0.054
Weight (Kg)	65.1 ± 11.7	62.0 ± 9.9	0.185
Height (cm)	168 ± 7.9	165 ± 8.2	0.092
BMI (Kg/m^2)	22.2 ± 2.9	21.7 ± 2.1	0.372
Waist (cm)	74.5 ± 8.9	71.9 ± 7.0	0.134

Table 2. Comparison of a series of parameters related to nutritional and lifestyle habits, depending on levels 25-HCC in the blood

	Insufficient levels n = 60	**Optimum levels n = 38**	**Value of p**
Coffee (%)	46.7	65.8	0.064
Alcohol (%)	30.0	26.3	0.694
Tobacco (%)	3.3	2.6	0.844
2 or more glasses of milk (%)	55.0	63.2	0.425
Meat 2 or more times/week (%)	76.7	76.7	0.534
Fish 2 or more times/week (%)	70.0	60.5	0.334
Butter (%)	8.3	5.3	0.565
Margarine (%)	6.7	15.8	0.146
Nº of salads weekly*	4 (3-5)	4 (2-5)	0.577
Nº of vegetables weekly*	3 (2-4)	3 (2-5)	0.950
Nº of fruits weekly*	6 (2-7)	7 (4-7)	0.223
Diet* in the last year (%)	18.3	23.7	0.522
Vitamin supplements (%)	21.7	7.9	0.072
Vitamin supplements in the last 3 months (%)	25.0	21.1	0.635
30 minutes walk daily (%)	76.7	76.3	0.968
Open air (walking) (%)	65.0	65.8	0.936
Sport (%)	51.7	55.3	0.728
Sport in open air (%)	11.7	21.1	0.408
Beach (last 3 months) (%)	71.7	63.2	0.377
Protective cream (%)	83.3	89.5	0.397
Hiking (%)	8.3	13.2	0.442
Rural living (%)	16.7	26.3	0.248
Chronic disease (%) ‡	30.0	31.6	0.869

(*) Median (IQR) ‡ The chronic diseases recorded were basically allergies (rhinitis, asthma), acne and migraine

Table 3. Biochemical parameters. Kidney function, liver function, blood lipids and ions

	Insufficient levels n = 60	Optimum levels n = 38	Value of p
Glucose (mg/dl)*	85 (82-88)	86 (81-91)	0.532
Urea (mg/dl)*	25 (22-28)	25 (22-32)	0.669
Creatinine (mg/dl)*	0.96 (0.89-1.07)	0.96 (0.89-1.04)	0.881
Uric acid (mg/dl)*	4.4 (3.7-5.3)	3.9 (3.3-4.8)	0.092
Total protein (g/L)*	7.5 (7.3-7.8)	7.6 (7.4-7.9)	0.478
Sodium (mEq/L)*	141 (140-142)	141 (140-142)	0.153
Potassium (mEq/L)*	4.3 (4.2-4.5)	4.3 (4.1-4.6)	0.921
HDL (mg/dL)	55.6 ± 14.0	58.3 ± 11.1	0.313
LDL (mg/dL)	104.8 ± 28.1	103.3 ± 24.7	0.779
Triglycerides (mg/dl)*	68 (53-107)	75 (59-91)	0.974
GPT (UI/L)*	15.7 (12.9-19.6)	15.3 (12.7-18.7)	0.904
GOT (UI/L)*	21.9 (20.0-24.6)	20.4 (16.6-23.2)	0.073
GGT (UI/L)*	15.6 (12.1-20.2)	14.3 (11.7-18.8)	0.314

(*) Median (IQR)

Table 4. Biochemical markers for remodelled bone. PTH and TSH

	Insufficient levels n = 60	Optimum levels n = 38	Value of p
FATR (UI/L)	2.1 (1.9-2.4)	2.0 (1.8-2.3)	0.255
Beta-crosslaps	0.46 (0.38-0.60)	0.46 (0.35-0.57)	0.699
P1NP (µg/L)	57.7 (44.3-74.3)	49.2 (41.4-68.7)	0.185
Osteocalcin (ng/mL)	24.3 (20.7-28.6)	24.2 (19.0-29.0)	0.930
TSH (UI/L)	1.84 (1.31-2.32)	1.60 (1.15-2.27)	0.284
PTH (ng/ML)	27.7 (20.1-34.8)	24.1 (16.0-34.1)	0.380

Median (IQR) in all cases

In this work we have studied what could be the factors which contribute to the existence of levels of 25-HCC below 30 ng/mL. Therefore, we have grouped the students according to their being below or above the cut-off point. The baseline characteristics of both groups are shown in Table 1. The same table shows that that is a higher number of males with low levels of vitamin D, the difference being statistically significant (p= 0.05), and confirmed in the logistic regression analysis (p= 0.047), Table 6. We did not observe statistically significant differences in any of the other variables shown in Table 1: age, height, weight, BMI or waist measurement. We do not know the reason why sex could play a role in the attainment, or not, of optimum levels of vitamin D. In a study carried out in healthy subjects, specifically 116 doctors starting their specialism (MIR), Calatayud et al.[27], confirmed the high prevalence of vitamin D insufficiency, since only 4.3% of the males and 12% of the females had levels of 25-HCC higher than 30 ng/mL. In another study carried out in Hawaii in young people, Binkley et al.[28], did not analyse the influence of sex on levels of 25-HCC, neither do they make reference to it, although the study included 60 males and 30

Table 5. Densitometric values in lumbar spine and proximal extremity of the femur. Ultrasound parameters in the calcaneum. Expressed as Z-score and T-score

	Level of vitamin D		
	Insufficient n = 60	Optimum n = 38	Value of p
DXA. Lumbar spine and proximal extremity of femur			
T-score lumbar	-0.125 ± 0.919	-0.135 ± 1.340	0.970
Z-Score lumbar	-0.104 ± 0.821	-0.103 ± 1.188	0.994
Z-Score femoral neck	0.209 ± 1.015	0.194 ± 1.209	0.947
T-Score femoral neck	0.151 ± 1.037	0.202 ± 1.194	0.823
T-Score total for hip	0.366 ± 1.114	0.265 ± 1.201	0.675
T-Score Trochanter	0.311 ± 1.073	0.314 ± 1.176	0.987
T-Score intertrochanter	0.368 ± 1.161	0.149 ± 1.147	0.364
Ultrasounds. Calcaneum			
Z-Score BUA	0.904 ± 0.774	0.904 ± 0.826	0.998
Z-Score SOS	1.372 ± 0.805	1.235 ± 0.823	0.483
Z-Score QUI	1.407 ± 1.032	1.184 ± 0.852	0.270
T-Score-BUA	-0.211 ± 0.781	0.903 ± 0.146	0.625
T-Score SOS	-0.097 ± 0.767	-0.199 ± 0.798	0.531
T-Score QUI	0.017 ± 1.030	-0.171 ± 0.858	0.351

The values express averages ± SD

Table 6. Multidimensional logistic analysis

Factor	Value of p	OR (95% CI)
Consumption of coffee	0.081	2.23 (0.91;5.50)
Hiking	0.058	4.51 (0.95;21.5)
Male sex	0.047	0.319 (0.103;0.985)
Vitamin supplements	0.048	0.233 (0.055;0.987)

females.

We did not find statistically significant differences in the distribution of lifestyle or nutritional habits between the two groups. In the comparison of averages or frequencies, we found only one "bias" in the consumption of coffee, which was less among students who had insufficient levels of 25-HCC, p= 0.064, and in the consumption of vitamin supplements which was higher in those students who had lower levels of vitamin D, p= 0.072. We did not find a single bibliographical reference around the possible reasons why a lower consumption of coffee is associated with lower levels of vitamin D, or the inverse, reasons why a higher consumption of coffee is associated with higher levels of vitamin D. Perhaps the only plausible explanation is that, in our culture, coffee is usually accompanied by milk, and the milk could be supplemented with vitamin D, but against this, we also observed in Table 2, that the consumption of milk was similar between the two groups, without statistically significant differences. We only found one study in the bibliography, published by Haney et al.[29], which, contrary to our study, associated the consumption of vitamin supplements with higher levels of 25-HCC.

Curiously, we did not find statistically significant differences between the students who had higher levels of 25-HCC with those who showed lower values, in any of the following variables: walking daily for 30 minutes, walking in the open air, practicing sport, practicing it in the open air, having been to the beach in the last three months, and use of protective creams. These findings surprised us, since we expected that the students who had higher levels of 25-HCC would have greater physical activity in the open air or have spent more time at the beach. In the study carried out with young people in Hawaii, the authors obtained results similar to ours[28].

We did not find statistically significant differences in any of the biochemical parameters which we analysed, which were measured, basically, to detect any asymptomatic pathology. The study by Hinkley et al.[29], also found no differences in the values of creatinine in the two groups of young people with higher and lower values of vitamin D. By being a population of healthy adults, in whom the existence of chronic disease was scarce, with a lower pathology (allergies, headaches, etc), there were no statistically significant differences in values of bone mineral density measured by double X-ray absorptiometry (DXA) or in ultrasound parameters in the calcaneum, as can be seen in Tables 3 and 5. For the same reason, no differences were found in the biochemical markers for remodelled bone, either for formation or for resorption, Table 4, or in levels of PTH.

Lastly, we carried out a logistic regression analysis, studying what variables are associated with levels of 25-HCC below 30 ng/mL, and we found a statistically significant association with the male sex (p= 0.04).

Among the limitations of our study we include the fact that it was a transversal study, with a relatively small population, as well as the fact that the collection of data on exposure to sun, lifestyles and nutritional habits was through self-completed questionnaires. It is possible that some students gave incorrect information on these matters. Finally, the 25-HCC was determined by immunochemiluminescence, which is the technique we had available, instead of high pressure liquid chromatography, which is considered to be the ideal technique for the measurement of this metabolite[30].

In conclusion, Canarian medical students, although being in ideal conditions for having optimum levels of vitamin D, showed high levels of insufficiency and deficiency, without our having been able to identify what factors are associated with this, with the exception of male sex. Therefore more studies are needed on this matter.

So, we need to look deeper into the causes which result in this "paradox", that in situations advantageous to the acquisition of vitamin D are found instances of insufficiency or deficiency in vitamin D.

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